The details of the proposed interference are set forth in the Remarks portion of this Amendment.

IN THE CLAIMS:

Please amend the claims as follows:

B1

33. (Amended) An apparatus for analyzing chemical species comprising:

(a) at least one vacuum pumping stage;

(b) an ion source for producing ions from a sample substance;

(c) at least one multipole ion guide located in at least one of said vacuum pumping stages;

(d) a mass analyzer;

(e) means for delivering ions from said ion source into said at least one multipole ion guide;

(f) means for applying voltages to said at least one multipole ion guide to direct said ions along a desired ion trajectory within said at least one multipole ion guide;

(g) means for applying additional voltages which impart energy to said ions within said at least one multipole ion guide so as to cause fragmentation of said ions located within said multipole ion guide;

(h) means to trap ions within said at least one multipole ion guide; and

(i) means to pulse a portion of said trapped ions into said mass analyzer.

Cancel claims 40, 54 and 55.

β2

57. (Amended) A method of analyzing chemical species utilizing an ion source, a vacuum system with at least one vacuum pumping stage, at least one multipole ion guide located in at least one of said vacuum pumping stages, and a mass analyzer, said method comprising:

(a) producing ions from a sample substance using said ion source;

(b) directing said ions into said multipole ion guide;

(c) fragmenting ions in said multipole ion guide to form an ion population in said multipole ion guide which contains fragment ions;

(d) trapping said fragment ions;

(e) pulsing a portion of said ion population which contains fragment ions toward said mass analyzer; and

(f) conducting mass to charge analysis of at least a portion of said ion population with said mass analyzer.

Please add the following new claims 66-120:

β3

66. An Apparatus for analyzing chemical species comprising;

(a) at least one vacuum pumping stage;

(b) an ion source for producing ions from a sample substance;

(c) at least one multipole ion guide located in at least one of said vacuum pumping stages;

(d) a Time-Of-Flight mass to charge analyzer;

(e) means for delivering said ions from said ion source to at least one multipole ion guide;

(f) means for applying electrical potentials to at least one multipole ion guide to select parent ions from said ions having a desired mass to charge ratio;

B3 Cont'd

(g) means for applying electrical potentials to at least one multipole ion guide to subject said parent ions to collision induced dissociation to generate fragment ions;

(h) means to trap said fragment ions and any remaining said parent ions in said at least one multipole ion guide;

(i) means to periodically release pulses of said trapped ions into said Time-Of-Flight mass to charge analyzer to detect said fragment ions with a second mass to charge ratio;

(j) means for providing a delay between the release of the said pulses of said trapped ions and initiation of pulses in the Time-of-Flight mass to charge analyzer; and

(k) means to adjust the delay to improve the duty cycle efficiency of said fragment ions with said second mass to charge ratio.

67. An apparatus according to claim 66, wherein said apparatus comprises at least two multipole ion guides with parent ions selected in one said multipole ion guide and ion fragmentation occurring in a second said multipole ion guide.

68. An apparatus according to claim 67, wherein said apparatus comprises means to accelerate said parent ions from said one multipole ion guide into said second multipole

B3 cont'd

ion guide to subject said parent ions to collision induced dissociation to generate fragment ions.

69. An apparatus according to claim 66, wherein said collision induced dissociation of said parent ions is caused by resonant frequency excitation.

70. An apparatus according to claim 66, wherein said collision induced dissociation of said parent ions is achieved by accumulating said parent ions in said at least one multipole ion guide while trapping said parent ions until fragmentation occurs.

71. An apparatus according to claim 66, wherein said apparatus comprises means to trap said parent ions in least one multipole ion guide, release said parent ions from the exit end of said at least one multipole ion guide, increasing the energy of said parent ions outside said internal volume of said at least one multipole ion guide, accelerating said ions back into said exit end of said at least one multipole ion guide wherein said accelerated ions collide with neutral background molecules in said internal volume of said at least one multipole ion guide generating said fragment ions that are trapped in said at least one multipole ion guide.

72. An apparatus according to claim 66, wherein a portion of said internal volume of said at least one multipol ion guide has a pressure in th range of 10^{-4} to 10^{-2} torr.

B3 cont'd

73. An apparatus according to claim 66, wherein a portion of said internal volume of said at least one multipole ion guide has a pressure in the range of 10^{-4} to 10^{-1} torr.

74. An apparatus according to claim 66, wherein said means to select parent ions comprises setting RF and DC electrical potentials applied to the electrodes of said at least one multipole ion guide.

75. An apparatus according to claim 66, wherein said means to select parent ions comprises applying resonant frequencies with single or multiple frequency notches to the electrodes of said at least one multipole ion guide.

76. An apparatus according to claim 66, wherein said means to select parent ions comprises setting or scanning RF amplitude electrical potentials applied to the electrodes of said at least one ion guide to reject unwanted ion mass to charge values.

77. An apparatus according to claim 66, wherein said means to select parent ions comprises applying resonant frequency excitation with RF and DC scanning to the electrodes of said multipole ion guide.

78. An apparatus according to claim 66, wherein said means to select ion mass to charge values and to fragment ions can be applied to the electrodes of at least one multipole ion guide to conduct single or multiple generation ion mass to charge selection and fragmentation st ps.

B3 Cont'd

79. An apparatus for analyzing chemical species comprising;

(a) at least one vacuum pumping stage;

(b) an ion source for producing ions from a sample substance;

(c) at least one multipole ion guide located in at least one of said vacuum pumping stages;

(d) a Time-Of-Flight mass to charge analyzer;

(e) means for delivering said ions from said at least one multipole ion guide;

(f) means for applying electrical potentials to said at least one multipole ion guide to select parent ions from said ions having a desired mass to charge ratio;

(g) means for applying electrical potentials to said at least one multipole ion guide to subject said parent ions to collision induced dissociation to generate fragment ions;

(h) means for applying electrical potentials to said at least one multipole ion guide to conduct ion mass to charge selection of fragment ions with subsequent fragmentation of selected ions;

(i) means for applying electrical potential to said at least one multipole ion guide to conduct single or multiple generation ion mass to charge selection and fragmentation;

(j) means to trap said fragment ions and any remaining said parent ions in said at least one multipole ion guide;

(k) means to periodically release pulses of said trapped ions into said Time-Of-Flight mass to charge analyzer to detect said fragment ions with a second mass to charge ratio;

B3 Cont'd

(l) means for providing a delay between the release of the said pulses of said trapped ions and initiation of pulses in the Time-of-Flight mass to charge analyzer; and

(m) means to adjust the delay to improve the duty cycle efficiency of said fragment ions with said second mass to charge ratio.

80. An apparatus for analyzing chemical species comprising;

(a) at least one vacuum pumping stage;

(b) an ion source for producing ions from a sample substance;

(c) at least two multipole ion guides located in at least one of said vacuum pumping stages;

(d) a Time-Of-Flight mass to charge analyzer;

(e) means for delivering said ions from said ion source into at least one multipole ion guide;

(f) means for applying electrical potentials to a first multipole ion guide to select at least one range of mass to charge values or parent ions; and

(g) means for applying electrical potentials to at least one multipole ion guide to subject said parent ions to collision induced dissociation to generate fragment ions in a second multipole ion guide.

81. An apparatus according to claim 80, wherein said apparatus comprises means to accelerate said par nt ions from said first multipol ion guide into said second multipole ion guide to subject said parent ions to collision induced dissociation to generate fragment ions.

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B3 cont'd

82. An apparatus according to claim 80, wherein said collision induced dissociation of said parent ions is caused by resonant frequency excitation.

83. An apparatus according to claim 80, wherein said collision induced dissociation of said parent ions is achieved by accumulating said parent ions while trapping said parent ions in said multipole ion guide until fragmentation occurs.

84. An apparatus according to claim 80, wherein said apparatus comprises means to accelerate said parent ions from said first multipole ion guide into said second multipole ion guide and means to apply resonant frequency excitation electrical potentials to said at least one multipole ion guide to achieve collision induced dissociation fragmentation of said parent ions.

85. An apparatus according to claim 80, wherein said apparatus comprises means to trap said parent ions in least one multipole ion guide, release said parent ions from one end of said at least one multipole ion guide, increasing the energy of said parent ions outside said internal volume of said at least one multipole ion guide, accelerating said ions back into said at least one multipole ion guide wherein said accelerated ions collide with neutral background molecules in said internal volume of said at least one multipole ion guide generating said fragment ions that are trapped in said at least one multipole ion guide.

β^3 cont'd

86. An apparatus according to claim 80, wherein a portion of said internal volume of at least one multipole ion guide has a pressure in the range of 10^{-4} to 10^{-2} torr.

87. An apparatus according to claim 80 wherein a portion of said internal volume of at least one multipole ion guide has a pressure in the range of 10^{-4} to 10^{-1} torr.

88. An apparatus according to claim 80, wherein said means to select parent ions comprises setting RF and DC electrical potentials applied to the electrodes of said first multipole ion guide.

89. An apparatus according to claim 80, wherein said means to select parent ions comprises applying resonant frequencies with single or multiple frequency notches to the electrodes of said first multipole ion guide.

90. An apparatus according to claim 80, wherein said means to select parent ions comprises setting or scanning RF amplitude electrical potentials applied to the electrodes of said multipole ion guide to reject unwanted ion mass to charge values.

91. An apparatus according to claim 80, wherein said means to select parent ions comprises setting or scanning RF amplitude electrical potentials and applying resonant frequency excitation to the electrodes of said multipole ion guide.

B3 Cont'd

92. An apparatus according to claim 80, wherein said means to select parent ions comprises setting or applying resonant frequency excitation with RF and DC scanning to the electrodes of said multipole ion guide.

93. An apparatus according to claim 80, wherein said means to select ion mass to charge values and to fragment ions can be applied to the electrodes of at least one multipole ion guide to conduct single or multiple generation ion mass to charge selection and fragmentation.

94. An apparatus according to claim 93, wherein said apparatus comprises means to conduct Time-Of-Flight mass to charge selection of the final fragment ion population or any generation of parent or fragment ions leading to the final fragment ion population.

95. An apparatus for analyzing chemical species comprising;

(a) at least one vacuum pumping stage;

(b) an ion source for producing ions from a sample substance;

(c) at least two multipole ion guides located in at least one of said vacuum pumping stages;

(d) a Time-Of-Flight mass to charge analyzer;

(e) means for delivering said ions from said ion source into at least on multipole ion guide;

(f) means for applying electrical potentials to a first multipole ion guide to select

B3 cont'd

at least one range of mass to charge values or parent ions;

(g) means for applying electrical potentials to a second of at least one multipole ion guide to subject said parent ions to collision induced dissociation to generate fragment ions in said second multipole ion guide;

(h) means to trap said fragment ions and any remaining said parent ions in at least one of said at least two multipole ion guides;

(i) means to periodically release pulses of said trapped ions into said Time-Of-Flight mass to charge analyzer to detect said fragment ions and any remaining said parent ions;

(j) means for providing a delay between the release of the said pulses of said trapped ions and initiation of pulses in the Time-of-Flight mass to charge analyzer; and

(k) means to adjust the delay to improve the duty cycle efficiency of said fragment ions.

96. An apparatus according to claim 95, wherein said means to select ion mass to charge values and fragment ions can be applied to conduct single or multiple generation ion mass to charge selection and fragmentation.

97. An apparatus according to claim 96, wherein said apparatus comprises means to conduct Time-Of-Flight mass to charge selection of the final fragment ion population or any generation of parent or fragment ions leading to the final fragment ion population.

B3 cont'd

98. An apparatus according to claim 95, wherein said apparatus comprises means to accelerate said parent ions from said first multipole ion guide into said second multipole ion guide to subject said parent ions to collision induced dissociation to generate fragment ions.

99. A method of effecting mass analysis on an ion stream, the method comprising;

1) of col. 19 line 56

(a) passing the ion stream through a first mass resolving spectrometer, to select parent ions having a first desired mass to charge ratio;

(b) subjecting the parent ions to collision induced dissociation to generate fragment ions;

(c) trapping the fragment ions and any remaining parent ions;

(d) periodically releasing pulses of the trapped ions into a Time-Of-Flight instrument to detect ions with a second mass to charge ratio; and

(e) providing a delay between the release of the pulses of trapped ions and initiation of pulses in the Time-Of-Flight instrument, and adjusting the delay to improve the duty cycle efficiency of ions with the second mass to charge ratio.

100. A method according to claim 99, which includes in step (a) sequentially stepping through a range of mass to charge values and detecting said fragment ions in said Time-Of-Flight instrument at each step, effectively scanning said first mass resolving spectrometer.

B3 Cont'd

101. A method according to claim 99, which includ s in step (a) st pping through a range of mass to charge values and detecting said fragment ions in said Time-Of-Flight instrument at each step, simultaneously adjusting said delay to optimize said duty cycle of a range of fragment ion mass to charge values that are specific neutral loss value relative to each parent ion selected, and acquiring a set of Time-Of-Flight mass spectra thereby effecting a neutral loss experiment.

102. A method according to claim 99, which includes the following additional steps:

sequentially setting the first mass resolving spectrometer to select non-contiguous parent ions with selected parent mass to charge ratios;

for each selected parent mass to charge ratio, adjusting the delay to optimize detection of a corresponding fragment ion in said Time-Of-Flight instrument;

whereby the acquired TOF spectra indicate the presence of each fragment ion generated from the corresponding parent ion, to effect a multipole reaction monitoring (MRM) experiment.

103. A method according to claim 99, which includes the releasing the pulses of trapped ions during a pulse period and adjusting the width of the pulse period, to improve the duty cycle efficiency for ions with the second mass to charge ratio.

B^3 Cont'd

104. A method according to claim 103, which includes adjusting the pulse period and the delay between the release of the pulses and initiation of the pulses in the Time-Of-Flight Instrument, to improve the duty cycle for a range of ion mass values, which includes said second mass to charge ratio.

105. A method of analyzing a chemical species utilizing an ion source, a vacuum system, at least two multipole ion guides, a Time-Of-Flight mass analyzer, said method comprising:

(a) producing ions from said chemical species in said ion source;

(b) directing said ions into at least one of said multipole ion guides;

(d) selecting parent ions having a first desired mass to charge ratio in at least one said multipole ion guide;

(e) subjecting said parent ions to collision induced dissociation to generate fragment ions in said second of at least two multipole ion guides; and

(f) conducting mass to charge analysis of a least a portion of said trapped population of ions with said Time-OF-Flight mass analyzer.

106. A method of analyzing a chemical species utilizing an ion source, a vacuum system, at least two multipole ion guides, a Time-Of-Flight mass analyzer, said method comprising:

(a) producing ions from said chemical species in said ion source;

(b) directing said ions into at l ast one of said multipole ion guides;

(d) selecting parent ions having a first desired mass to charge ratio in one said

B3 cont'd

multipole ion guide;

(e) subjecting said parent ions to collision induced dissociation to generate fragment ions in a second of said at least two multipole ion guides;

(f) trapping the fragment ions and any remaining parent ions in said at least one of said multipole ion guides;

(g) periodically releasing pulses of said trapped ions into said Time-Of-Flight instrument to conduct ion mass to charge analysis; and

(h) providing a delay between the release of the pulses of said trapped ions and initiation of pulses in said time of flight instrument, and adjusting said delay to improve the duty cycle efficiency of said ions mass to charge analyzed.

107. An apparatus according to claim 106, wherein said apparatus comprises means to accelerate said parent ions from said one multipole ion guide into said second multipole ion guide to subject said parent ions to collision induced dissociation to generate fragment ions.

108. A method of analyzing a chemical species utilizing a chemical separation system, an ion source, a vacuum system with at least one vacuum pumping stage, at least one multipole ion guide, a Time-Of-Flight mass analyzer, said method comprising:

(a) directing a peak of ion species eluting from said chemical separation system into said ion source;

(b) producing ions from said chemical species in said peak in said ion source;

(c) directing said ions into at least one of said multipol ion guides;

B3 Cont'd

(d) trapping said ion species from said peak in said at least one multipole ion guide;

(e) conducting single or multiple ion mass to charge selection and fragmentation steps of said trapped ions producing a population of ions; and

(f) conducting mass to charge analysis of a least a portion of said trapped population of ions with said Time-OF-Flight mass analyzer.

109. A method according to claim 108, wherein the delay between the release of the pulses of trapped ions and initiation of pulses in the time of flight instrument is optimized to improve the duty cycle efficiency of said population of ions analyzed by said Time-Of-Flight mass analyzer.

110. A method according to claim 108, wherein said chemical separation system comprises a liquid chromatography system.

111. A method according to claim 108, wherein said chemical separation system comprises a capillary electrophoresis system.

112. A method to generate an MS/MS spectra comprising the steps:

(a) acquiring a parent ion mass to charge spectrum;

(b) fragmenting a selected parent ion species using resonant frequency excitation collision induc d dissociation to produce a population of fragment ions and remaining parent ions;

B^3 Cont'd

(c) acquiring a second ion mass to charge spectrum of said population of fragment ions and remaining parent ions; and

(d) subtracting said parent ion mass to charge spectrum from said second ion mass to charge spectrum resulting in a third ion mass to charge spectrum containing peaks of fragment ions.

113. A method to generate an MS/MS/MS spectra comprising the steps:

(a) acquiring a first ion mass to charge spectrum containing first generation fragment ions and remaining parent ions by applying resonant frequency excitation to cause collision induced dissociation resulting in fragmentation of a selected parent ion species;

(b) acquiring a second ion mass to charge spectrum containing second generation fragment ions and remaining first generation fragment ions and parent ions by applying multiple frequency resonant frequency excitation to cause collision induced dissociation of selected parent and first generation fragment ion species; and

(c) subtracting said second from said first ion mass to charge spectrum resulting in a third ion mass to charge spectrum containing peaks of second generation fragment ions.

114. A method to generate an MS/MS^n spectra comprising the steps:

(a) acquiring a first ion mass to charge spectrum containing –1 generation fragment ions and any remaining parent ions and first generation fragment ions through –2 generation fragment ions by applying multiple frequency resonant

B3 Cont'd

frequency excitation to cause collision induc d dissociation of selected parent and first generation fragment through −2 generation fragment ions;

(b) acquiring a second ion mass to charge spectrum containing n generation fragment ions and any remaining parent ions and first generation fragment ions through −1 generation fragment ions by applying multiple frequency resonant frequency excitation to cause collision induced dissociation of selected parent and first generation fragment through −1 generation fragment ions; and

(c) subtracting said second from said first ion mass to charge spectrum resulting in a third ion mass to charge spectrum containing peaks of n generation fragment ions.

115. A method of effecting mass analysis on an ion stream, the method comprising:

(a) passing the ion stream through a first mass resolving spectrometer, to select parent ions having a first desired mass-to-charge ratio;

(b) subjecting the parent ions to collision-induced dissociation to generate fragment ions;

(c) trapping the fragment ions and any remaining parent ions;

(d) periodically releasing pulses of the trapped ions into a time of flight instrument to detect ions with a second mass-to-charge ratio; and

(e) providing a delay between the release of the pulses of trapped ions and initiation of push-pull pulses in the time of flight instrument, and adjusting the delay to improve the duty cycle efficiency of ions with the second mass-to-charge ratio.

no step one

116. A method as claimed in claim 115, which includes in step (1) sequentially scanning over a range of masses, to effect a parent ion scan.

117. A method as claimed in claim 115, which includ s scanning the first and second mass-to-charge ratios over desired ranges to maintain a substantially constant neutral mass loss between the first and second mass-to-charge ratios, whereby a neutral loss scan is effected, and simultaneously adjusting the delay as the second desired mass-to-charge ratio is scanned over the desired range.

B3 cont'd

118. A method as claimed in claim 115, which includes the following additional steps:

(a) sequentially setting the first mass resolving spectrometer to select non-contiguous parent ions with selected parent mass-to charge ratios;

(b) for each selected parent mass-to charge ratio, adjusting the delay for detection of a corresponding fragment ion; and

(c) whereby the TOF spectra indicate the presence of each fragment ion generated from the corresponding parent ion, to effect a multiple reaction monitoring (MRM) scan.

119. A method as claimed in claim 115, which includes releasing the pulses of trapped ions during a pulse period and adjusting the width of the pulse period, to improve the duty cycle efficiency for ions with the second mass-to-charge ratio.

120. A method as claimed in claim 119, which includes adjusting the pulse period and the delay between the release of the pulses and initiation of the push-pull pulses in the time of flight instrument, to improve the duty cycle for a range of ion mass values, which includes said second mass-to-charge ratio.